

## ABSTRACT

Human bone marrow-derived stem cells are differentiated into pancreatic endocrine marker-expressing cells in vitro by first culturing human bone marrow mononuclear cells in a tissue culture container to obtain cells that adhere to the container, and continuing to culture  
5 the adherent cells until they become morphologically homogenous; second, culturing the morphologically homogeneous cells in a medium containing high glucose levels at least until the cells express detectable levels of glucagon, insulin, and mRNAs encoding insulin, Pdx-1, and NeuroD; and third, culturing the cells in a medium containing low glucose levels, nicotinamide, and exendin 4. Transplantation of pancreatic endocrine marker-expressing  
10 cells made in this manner can reduce hyperglycemia in a diabetic animal.